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10/006,760	11/19/2001	Shohei Koide	176/60901 (6-11402-968)	2042

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EXAMINER	
SHAFER, SHULAMITH H	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/006,760	KOIDE, SHOHEI	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-16,145-183 and 185* is/are pending in the application.

4a) Of the above claim(s) *145-180* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-16,181-183 and 185* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Applicant's amendments and remarks of 9 October 2007, in response to the 10 April 2007 Office Action, are acknowledged and have been entered.

In response to the election of species requirement set forth in previous Office Action, applicant elects SEQ ID NO:23 as the BC loop region sequence, SEQ ID NO:34 as the AB loop region sequence and SEQ ID NO:67 as the FG loop region sequence.

Claims 1 and 9 have been amended. Claims 1-11, 13-16, 145-183 and 185 are pending in the instant application. Claims 145-180 are withdrawn as drawn to non-elected inventions. Claims 1-11, 13-16, 181-183 and 185 are under consideration to the extent they read on the elected invention.

Information Disclosure Statement:

The information disclosure statement filed 5 December 2007 has been considered. Reference 1 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it is a duplicate of reference submitted on a previous IDS (10 April 2007). It has been lined through and not considered, since a reference may appear only once on the face of a patent.

Withdrawn Rejections

The rejection of Claims 1-11, 13 and 14 under 35 U.S.C. 102(b) as being anticipated by Pasqualini et al. (13 July 1999. US 5,922,676, the '676 patent) is withdrawn in view of applicant's amendment to the claims.

The rejection of Claims 1-11, 13-15, and 185 under 35 U.S.C. 102(b) as being anticipated by Koide (1998. WO 98/56915, cited on IDS) is withdrawn in view of applicant's arguments.

Maintained/New Rejections and/or Objections

Objections:

Claims 181-183 are objected to as reciting non-elected species. Appropriate correction is required.

Double Patenting:

The rejection of Claims 1-11, 13-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent No. 6,673,901 in view of Lipovsek et al (US 6,818,418 filed, 29 February 2000) is maintained for reasons of record and now applied to claim 185.

Applicant traverses this rejection (Remarks, 9 October 2007, page 10 paragraph 4). The reason for the traversal is that while claim 1 of the '901 patent is generic to the presently claimed subgenus, neither Koide nor Lipovsek teach or suggest the presently claimed subgenus, a modified loop region that affords a polypeptide having nuclear receptor binding activity.

Applicant's arguments have been fully considered but are not found to be persuasive for reasons of record. Claim 1 of the '901 patent recites a fibronectin type III (Fn3) polypeptide monobody that binds to a specific binding partner (SBP) to form a polypeptide:SBP complex. The monobody is designed on the basis of a scaffold of wild-type 10th Fn3 domain of fibronectin (page 32, lines 3-5), which is identical to SEQ ID NO:2 of the instant invention. Claim 1 and the specification of the '901 patent fail to further define, or identify examples of "specific binding partner(s)". Thus, the '901 patent does not teach any "specific binding partner". The '418 patent teaches protein variants of the tenth module of human Fn3, the protein of SEQ ID NO:2 of the instant invention. The protein taught by the '418 patent is characterized by its ability to bind to a compound that is not bound by the corresponding naturally-occurring fibronectin (column 2, lines 32-36). As an example of a binding compound, the '418 patent teaches

receptor/ligand pairs (column 5, line 39). The receptor can be considered to encompass nuclear receptors.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of the '901 patent to obtain a fibronectin type III monobody which binds a "specific binding partner" (as taught by the 901 patent) wherein the specific binding partner is a receptor/ligand pair, encompassing a nuclear receptor, as taught by the '418 patent. The person of ordinary skill in the art would have been motivated to make these modifications and have expected success because both the '901 and the '418 patents teach polypeptides which are variants on fibronectin type III (Fn3) polypeptide which bind compounds that are not bound by naturally-occurring fibronectin.

Therefore, the monobody of the instant invention is an obvious variation of the monobody set forth in the claims of the '901 patent in view of the teachings of the '418 patent.

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 1-11, 13-16, 181-183 and 185 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record and for reasons set forth below.

Claims 1, 9-11, and 185 are vague and indefinite in reciting "the loop region sequence being selected for the group of loops AB, BC, CD, DE, EF, FG and combinations thereof....." (Claim 1), "the combination of ....." (Claim 9), "and combinations thereof" (Claim 10), " a combination of the BC loop region sequence and the FG loop region sequence" (claim 11), and "loop region sequences selected from the group of AB, BC, FG, and combinations thereof....." (Claim 185). It is unclear what applicant intends by combinations or combinations thereof; one cannot determine how

many loops are to be in the combinations. It is unclear if a combination is to be one (large) loop comprising the sequences of several recited loop sequences, or a monobody comprising one or more loop region sequences linked between adjacent β-strand domain sequences.

Applicant traverses the rejection (Response of 9 October 2007, page 10, last paragraph). The reason for the traversal is that the language is not unclear and is explicitly disclosed in Table 1 of the specification where species having modified BC and FG loops are described.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

While the claims are to be interpreted in light of the teachings of the specification, it is improper to read limitations or embodiments of the specification into a claim (See MPEP 2111.01). The claims, as recited, fail to distinguish between a large loop which is a combination comprising the sequences of several recited loop sequences, or a monobody comprising one or more of the recited loop region sequences between adjacent β-strand domain sequences.

Claim 1 is vague and indefinite in reciting "monobody derived from the amino acid sequence ...". It is unclear if applicant intends a monobody that is a modification of the Fn3 polypeptide of SEQ ID NO:2 or 3 or a protein which is obtained from another protein or something else entirely.

Claim 1 recites "optionally, an N-terminal tail of at least about 2 amino acids, a C-terminal tail of at least about 2 amino acids, or both." It is unclear if applicant intends the full length fibronectin molecule to meet the limitations of the claim, since the claim does not recite an upper limit to the number of amino acids at the N- or C- termini.

Claims 1 and 185 recite "wherein at least one loop region sequence ..... comprises an amino acid sequence which varies by deletion, insertion or replacement of at least two amino acids from a corresponding loop region.....". It is unclear if applicant intends to delete or replace an entire loop region of the monobody, or insert an additional loop sequence, since no upper limit to the number of amino acids to be deleted, inserted or replaced is recited.

Claims 1, 9-11, and 185 are vague and indefinite in reciting various loop region sequences (i.e. AB, BC, CD, etc.). It is unclear what portion of the Fn3 sequence is encompassed by the term "loop region sequences"; therefore, the metes and bounds of the claims cannot be determined.

Applicant has not responded to these rejections which were made in previous office action (10 April 2007); therefore the rejections are maintained for reasons of record.

Claims 2-8, 13-16 and 181-183 are included in this rejection as depending from rejected claims.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13-16, 181-183 and 185 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fibronectin type III (Fn3) polypeptide monobody derived from amino acid sequence of SEQ ID NO:2 or SEQ ID NO:3, wherein the monobody loop regions comprise the residues 15-16 of the AB loop, residues 22-30 of the BC loop and residues 76-87 of the FG loop varying by substitutions, insertions or replacement of 2 to 25 amino acid residues, and wherein the replaced loop region amino acid residues bind to nuclear receptor, does not reasonably provide enablement for a fibronectin type III polypeptide monobody comprising a monobody wherein any amino acids in any loop regions other than AB, BC or FG loops have any amino acid deletions, insertions, or replacements. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include,

but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.1988).

The claims are broadly drawn to a monobody derived from amino acid sequences of SEQ ID NO:2 or 3 comprising at least two adjacent Fn3 beta-strand sequences with any loop sequence comprising an amino acid sequence which varies by deletion, insertion or replacement of at least two amino acids from the corresponding loop region. Thus, the loop region may vary by two up to an indefinite number of amino acid residues, or may be deleted entirely. The claims encompass a monobody in which all of the amino acids of the wild-type loop sequence are replaced.

The specification teaches wild type (SEQ ID NO:2) and mutant (SEQ ID NO:3) Fn3 scaffolds characterized by seven beta-strand domain sequences (designated A through G) and six loop regions (AB loop, BC loop, CD loop, DE loop, EF loop, and FG loop) which connect the seven beta-strand domain sequences. In SEQ ID Nos: 2 and 3, the AB loop corresponds to residues 15-16, the BC loop corresponds to residues 22-30, the CD loop corresponds to residues 39-45, the DE loop corresponds to residues 51-55, the EF loop corresponds to residues 60-66, and the FG loop corresponds to residues 76-87 (page 14, lines 18-25). The disclosure teaches "deletions can be a deletion of at least two amino acid residues up to about 25 amino acid residues, ...Replacements can be replacements of at least two up to substantially all amino acid residues appearing in a particular loop region or tail...." (page 15, lines 17-22). There is insufficient guidance presented in the specification as to the type of changes that may be made in any or all the loops which would result in a monobody that retains the required activity: nuclear receptor binding activity.

The working examples (examples 1 and 2) teach making loops comprising the following variations: (a) insertion of seven diversified residues between Pro-15 and Thr-16 in the AB loop (page 37, lines 15-17 and Table 2); (b) diversifying residues 26-30 in the BC loop (page 37, line 13 and Table 1) and; (c) randomizing residues 78-85 and

inserting an additional eight randomized residues in the FG loop (page 37, lines 17-19, and Tables 1, 3 and 4). There are no examples, working or prophetic, of monobodies comprising variant CD, DE, or EF loops or other variants which retain the required activity.

Applicant has not disclosed which portions of a given loop sequence, ie which amino acid positions, must be maintained, and which may be changed to render the monobody capable of binding nuclear receptors. While the starting scaffold may be disclosed, insufficient guidance is presented in the specification as to the changes which may or may not be made in the loop sequences that would result in a monobody capable of binding a nuclear receptor, or a nuclear receptor that has bound a particular agonist or class of agonists, or a nuclear receptor which has been bound by a particular antagonist or class of antagonists. The monobodies of the instant invention could potentially bind proteins other than the nuclear receptor. Thus, these monobodies may bind any number of proteins of widely diverse biological activity. Absent sufficient guidance as to which amino acids in which of the loops of the monobody could be altered, undue experimentation would be required to make the monobodies that specifically bind nuclear hormones.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein with the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequences are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al 1990. Science 247:1306-1310). Although the specification outlines art-recognized procedures for producing and screening for active protein variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to

use the current invention as a starting point for further experimentation. The specification only teaches how to screen for claimed monobodies and test for functional variants.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives based on variants of any recited loop region sequences and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required to provide activity, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of Claims 1-11, 13, 14, and 185 under 35 U.S.C. 102(e) as being anticipated by Lipovsek et al. (16 November 2004. US 6,818,418, filed 29 Feb. 2000, the '418 patent) is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (Response of 9 October 2007, page 12). The reasons for the traversal are: Lipovsek does not teach a polypeptide that exhibits nuclear receptor binding affinity; the polypeptides of taught by Lipovsek and those claimed in the instant invention have a genus-species relationship; one would not envisage the subgenus claimed by the instant invention.

Applicant's arguments have been carefully considered but have not been found to be persuasive. The claims of the instant invention are broadly drawn to a polypeptide comprising a Fn3 domain; this is the protein domain taught as a scaffold for the antibody mimics of the '418 patent. The modifications recited in the claims of the instant invention comprise modifications in at least one loop region (the loop region is not further specified); said modifications comprise an amino acid sequence which varies by deletion, insertion or replacement of at least two amino acids from a corresponding loop region. Thus, the claims encompass any number of unspecified modifications to the Fn3 polypeptide, including insertion or deletion of an entire loop region. There are no structural limitations to the modified loop regions. The claims recite only a functional limitation: that the modified monobody exhibit nuclear receptor binding activity. The '418 patent teaches a protein having at least one randomized loop (modification), the protein being characterized by its ability to bind to a compound that is not bound by the corresponding naturally-occurring fibronectin (column 2, lines 32-36). The reference teaches that the fibronectin-based molecules may be used as scaffolds which are subjected to directed evolution; such directed evolution approach results in the production of antibody-like molecules with high affinities for a protein of interest, that is a potential binding partner (column 2, lines 13-23). Thus, the '418 patent teaches polypeptides designed to bind any specific binding partner and methods of making said polypeptides. Among the compounds taught by the '418 patent as possible binding partners are receptor/ligand pairs, including hormone receptor/ligands (column 5, lines 34-49). The claims of the instant invention do not recite specific structural characteristics of a monobody that would exhibit the characteristics of binding a nuclear receptor, other than modifications in the loop regions. The '415 patent teaches polypeptides comprising modified loop regions, said modifications enabling the protein to bind a specific polypeptide that is not bound by the corresponding naturally-occurring fibronectin. Since the '415 patent teaches polypeptides designed to bind receptor/ligand pairs, including hormone receptor/ligands, one of ordinary skill in the art would recognize that the teachings of the '415 patent encompass polypeptides

designed to specifically bind the nuclear receptors and cognate ligands of the claimed invention. Therefore, the rejection is maintained.

35 U.S.C. § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11, 13-15 and 185 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koide (1998. WO 98/56915) in view of Lipovsek et al. (16 November 2004. US 6,818,418, filed 29 Feb. 2000, the '418 patent).

As discussed above, the claims of the instant invention are broadly drawn to a modified polypeptide comprising a Fn3 domain. The modifications recited in the claims of the instant invention comprise modifications in at least one loop region (said loop region is unspecified); said modifications comprise an amino acid sequence which varies by deletion, insertion or replacement of at least two amino acids from a corresponding loop region. Thus, the claims encompass any number of unspecified modifications to the Fn3 polypeptide, including insertion or deletion of an entire loop region.

Koide teaches a fibronectin type III (Fn3) polypeptide monobody. The monobody is designed on the basis of a scaffold of wild-type 10th Fn3 domain of fibronectin (page 32, lines 3-5), which is identical to SEQ ID NO:2 of the instant invention. The WO document teaches a polypeptide monobody comprising a plurality of Fn3 β-strand domain sequences that are linked to a plurality of loop region sequences. One or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3. One or more of the loop regions of the monobody

comprise amino acid residues of the AB loop, the BC loop, the CD loop, the DE loop, the EF loop and the FG loop (page 6, lines 12-26). The WO document teaches fusion proteins comprising His-tags (page 21, line 4). The monobody is disclosed as capable of binding to a specific binding partner (abstract and page 8, lines 8-10). The specific binding partner of the Koide reference is not further identified or characterized. The modifications of the loop regions, which would result in a monobody capable of binding a "specific binding partner" are not further disclosed. Thus, the teachings of the WO document are broadly directed to unspecified modifications of the loop regions of the Fn3 polypeptide such that the polypeptide will bind a specific binding partner, which is not further identified. Thus, Koide does not teach a specific binding partner wherein the binding partner is a nuclear receptor.

The '418 patent teaches protein variants of the tenth module of human Fn3, the protein of SEQ ID NO:2 of the instant invention. The protein taught by the '418 patent is characterized by its ability to bind to a compound that is not bound by the corresponding naturally-occurring fibronectin (column 2, lines 32-36). As discussed above, the '418 patent teaches that the fibronectin-based molecules may be used as scaffolds which are subjected to directed evolution; such directed evolution approach results in the production of antibody-like molecules with high affinities for proteins of interest, that is potential binding partners. Thus, the '418 patent teaches polypeptides designed to bind any specific binding partner and methods of making said polypeptides. As an example of a binding compound, the '418 patent teaches receptor/ligand pairs including hormone receptor/ligands (column 5, line 39). One of ordinary skill in the art would recognize that hormone/receptor ligand pairs would encompass the nuclear receptors and the cognate ligands of the claimed invention.

Thus, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of Koide, which teach a monobody with unspecified modifications in the loop regions, said modifications allowing the monobody to bind an unidentified specific binding protein, and the '418 patent, which teaches antibody mimics specifically designed to bind polypeptides of interest, wherein the polypeptides of interest comprise receptor/ligand pairs, including

hormone receptor/ligands (and teaches methods of producing said antibody mimics by directed evolution) and modify the monobody taught by Koide, so that the loops of the monobody are modified to bind a specific binding partner wherein said specific binding partner is a hormone receptor/ligand pair as taught by the '418 patent. One of ordinary skill in the art would have been motivated to make this modification because Koide teaches monobodies, with unspecified structural characteristics that bind specific, but not further identified binding partners and the '418 patent teaches that hormone receptor/ligand pairs are among the binding partners encompassed by the patent. One would have anticipated success because both of the references teach making variants of fibronectin type III polypeptides to bind compounds not bound by naturally-occurring fibronectin, and the '418 patent teaches a directed evolution approach which results in the production of antibody-like molecules with high affinities for proteins of interest, including receptors.

Claims 181-183 are free of the prior art.

Doucette-Stamm et al (2002, US 6,380,370, filed 13 August 1998) teach a sequence, SEQ ID NO:4375 of a 98 amino acid polypeptide which comprises a sequence (residues 48-52) that is 100% identical to SEQ ID NO:23 of the instant invention. The sequence comprises a *Staphylococcus epidermis* polypeptide which may be used in diagnosis and treatment of bacterial infections. The reference does not anticipate or render obvious the claim 181 of the instant invention, a polypeptide monobody wherein the BC loop region sequence comprises the amino acid sequence of SEQ ID NO:23

Drmanic et al (WO200175067, priority claimed to 31 March 2001) teaches a polypeptide, SEQ ID NO:39760, a 285 amino acid polypeptide that comprises a fragment that is 54.8% identical to SEQ ID NO:67 of the instant invention. The polypeptide is described as a novel human diagnostic amino acid sequence. The reference does not anticipate or render obvious the substitutions in the fragment necessary to arrive at SEQ ID NO:67 of the instant invention.

Breton et al. (2003. US 6610836, filed 27 January 2000) teaches a 239 amino acid polypeptide, SEQ ID NO:13019, which comprises a fragment that is 93.9% identical to SEQ ID NO:34 of the instant invention. The polypeptide is described as a *Klebsiella pneumoniae* polypeptide. The reference does not anticipate or render obvious the substitutions in the fragment necessary to arrive at SEQ ID NO:34 of the instant invention.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/

Primary Examiner, Art Unit 1647

/S. H. S./

Examiner, Art Unit 1647